

Heart Failure Council of Thailand (HFCT) 2019 Heart Failure Guideline: Atrial Fibrillation in Heart Failure Guidelines

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Atrial fibrillation (AF) and heart failure (HF) often coexist. Nearly 40% of patients hospitalized for HF have a history of AF, and up to 50% of patients have AF at baseline. Additionally, 20% of patients may experience new-onset AF during hospitalization. Heart failure patients with AF tend to be older, more frequently females, and they have a higher prevalence of coronary artery disease, and a higher prevalence of valvular heart diseases or chronic non-cardiac diseases compared to HF patients without AF. The prevalence of AF increases commensurately with increasing severity of HF, from 5% in patients with New York Heart Association (NYHA) Functional Class I symptoms to nearly 50% in NYHA Functional Class IV patients⁽¹⁾.

Heart failure has been identified as an independent risk factor for the occurrence of AF [hazard ratio (HR) 3.20, 95% confidence interval (CI) 1.99 to 5.16].

Impact

AF precipitates HF, and vice versa. AF during HF can be very difficult to manage, and it limits the

use of several treatment options. In AF patients, the development of HF was associated with increased mortality (HR 2.7, 95% CI 1.9 to 3.7 for men versus HR 3.1, 95% CI 2.2 to 4.2 for women). In HF patients, the development of AF was also associated with increased mortality (HR 1.6, 95% CI 1.2 to 2.1 for men versus HR 2.7, 95% CI 2.0 to 3.6 for women). The two most common underlying cardiac disorders in patients presenting with stroke are AF and HF, which are observed in 15% and 9% of all strokes, respectively. Eighty two percent of all strokes that occur in patients with coexisting HF and AF are cardioembolic^(2,3). Current data suggest an equal level of stroke risk between HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF).

Chronic HFrEF is commonly induced by high ventricular rate AF or by frequent premature ventricular contractions (PVCs). In an AF setting, treatment of the arrhythmia (i.e., rhythm control with cardioversion, antiarrhythmic drugs or AF ablation, or rate control with drugs or ‘ablate and pace’ strategy) usually improves left ventricular (LV) function. In some patients with chronic AF and reduced LV function, AV junction ablation with permanent pacing may be the only treatment option. Accumulating data are suggesting that the regularity of ventricular contraction, not only the rate, may play a role in the development of tachycardia-induced cardiomyopathy^(4,5).

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Table 1. Stroke prevention in patients with AF in HF

Patient with HF and AF with	NOAC	Warfarin	Aspirin alone
Men: CHA ₂ DS ₂ -VASc=1 Woman: CHA ₂ DS ₂ -VASc=2	IIa	IIa	III
Men: CHA ₂ DS ₂ -VASc ≥2 Woman: CHA ₂ DS ₂ -VASc ≥3	I	I	III
Moderate-to-severe mitral stenosis or mechanical heart valves	III	I	III

AF=atrial fibrillation; HF=heart failure; NOAC=non-vitamin K antagonist oral anticoagulants

Table 2. Recommendations regarding the management of acute AF in patients with HF

Recommendation	COR	LOE
Electrical cardioversion is recommended in patients with acute AF that have unstable vital signs, ongoing ischemia, and signs of significant heart failure (e.g., pulmonary edema or respiratory failure).	I	A
Anticoagulant is recommended after cardioversion in patients with acute AF.	I	A
Treatment of other comorbidities, such as CAD, HF, and OSA, is recommended.	I	A
Fluid balance should be monitored.	IIa	C
Heart rate control to less than 110 bpm.	I	A
Pharmacologic cardioversion with amiodarone is recommended in patients with HFrEF that develop mild HF.	I	A

AF=atrial fibrillation; CAD=coronary artery disease; COR=class of recommendation; HF=heart failure; HFrEF=heart failure with reduced ejection fraction; LOE=level of evidence; OSA=obstructive sleep apnea

Management

The 2016 European Society of Cardiology (ESC) AF guidelines recommend the initial use of CHA₂DS₂-VASc score to identify patients at low risk of stroke that do not require any type of antithrombotic treatment. Patients with one or more risk factors for stroke can be offered effective stroke prevention with either vitamin K antagonists (VKAs) or non-VKA oral anticoagulants (NOACs)⁽⁶⁾ (Table 1).

Prevention

Retrospective analyses of large randomized trials reported a lower incidence of new-onset AF in patients treated with Angiotensin converting enzyme inhibitors (ACEIs) or Angiotensin II receptor blockers (ARBs) compared to those treated with placebo. The lesser degree of reduction in the incidence of AF is observed in patients with heart failure with preserved ejection fraction (HFpEF) treated with ACEIs/ARBs. This treatment has no effect at all in patients without heart failure. Nephilysin inhibitor does not seem to add any benefit on the reduction of AF. Beta-blocker therapy was associated with a 33% reduction in the adjusted odds of incident AF in HFrEF patients pretreated with ACEIs/ARBs, which reinforces the importance of beta-blocker therapy in HFrEF patients with sinus rhythm. Eplerenone, a mineralocorticoid receptor

antagonist (MRA), also reduced the risk of new-onset AF in patients with LVEF of 35% or less (NYHA Functional Class II) when added to ACEIs/ARBs and beta-blockers^(7,8) (Table 2). Recommendations regarding stroke prevention in patients with AF in HF being treated with oral anticoagulant (OAC) and left atrial appendage (LAA) occluder device is shown in Table 3.

There is no direct evidence in favor of rhythm control strategy over rate control in patients with coexisting AF and HF. Data from randomized trials suggest no difference in cardiovascular mortality, all-cause death, or worsening of HF between the two strategies in AF patients with HF. This absence of differences among outcomes between rhythm and rate control is mostly due to proarrhythmic side effects. The guidelines recommend that AF management in HF patients should commonly start with rate control, with rhythm control being subsequently attempted in cases with persistent AF symptoms. Lenient heart rate control with beta-blocker during AF (of less than 110 bpm) should be the target. Digitalis, preferably in combination with beta-blocker, should be considered the second-line treatment strategy. Amiodarone may be used for rate control if beta-blocker and digitalis are not effective (Table 4).

Catheter ablation (CA), whether pulmonary

Table 3. Recommendations regarding stroke prevention in patients with AF in HF being treated with oral anticoagulant (OAC) and left atrial appendage (LAA) occluder device

Recommendation	COR	LOE
Risk stratification by CHA ₂ DS ₂ -VASc and HAS-BLED scores is recommended	I	A
Oral anticoagulant is recommended in patients with a CHA ₂ DS ₂ -VASc score of 2 or more in males, and 3 or more in females.	I	A
Patients with a CHA ₂ DS ₂ -VASc score of 1 in males, and 2 in females should receive oral anticoagulant according to individual characteristics and patient preferences.	IIa	A
Vitamin K antagonist therapy (INR 2.0-3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valve.	I	B
When oral anticoagulation is initiated in a patient with AF that is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is preferred.	I	A
When patients are treated with a vitamin K antagonist, time in therapeutic range (TTR) should be kept as high as possible and closely monitored.	I	A
Combinations of OAC and antiplatelet increase bleeding risk and should be avoided unless another specific indication for platelet inhibition.	III	B
In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention.	III	B
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III	A
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (LOE: B) or moderate-to-severe mitral stenosis (LOE: C).	III	B/C

AF=atrial fibrillation; COR=class of recommendation; INR=international normalized ratio; LOE=level of evidence; NOACs=non-vitamin K antagonist oral anticoagulants; OAC=oral anticoagulants; TTR=time in therapeutic range

Table 4. Recommendations regarding rate and rhythm control in patients with AF in HF

Recommendation	COR	LOE
Heart rate control is recommended in AF patients with LVEF ≥40% that are taking either beta-blocker, digoxin, diltiazem, or verapamil or a combination of these agents.	I	B
Beta-blocker and digoxin are recommended in AF patients with LVEF <40%.	I	B
In patients with hemodynamic instability or severely depressed LVEF, amiodarone may be considered for acute control of heart rate.	IIb	B
Lenient rate control (a resting heart rate of <110 bpm) should be considered the target in heart rate control therapy.	IIa	B
Rhythm control is preferred over rate control in pre-excited AF and AF during pregnancy.	IIa	C
Atrioventricular node ablation should be considered to control heart rate in patients unresponsive or intolerant to intensive rate and rhythm control therapy, accepting that these patients will become pacemaker dependent.	IIa	B
Consider early low-dose combination therapy of beta-blocker and digitalis as initial therapy.	IIa	B
Long-term rhythm control with amiodarone is recommended if it is determined that the benefits outweigh the risks.	I	A
Catheter ablation for rhythm control may be considered in some paroxysmal and persistent AF patients with HFrEF.	IIa	B
Dronedronarone, flecainide, and propafenone are not recommended in HFrEF as a rhythm control strategy.	III	A

AF=atrial fibrillation; COR=class of recommendation; HFrEF=heart failure with reduced ejection fraction; LOE=level of evidence; LVEF=left ventricular ejection fraction

vein isolation or His ablation of AF plus pacemaker implantation, in HF patients may be considered when amiodarone fails to control symptoms (Figure 1). Two meta-analyses showed no difference between

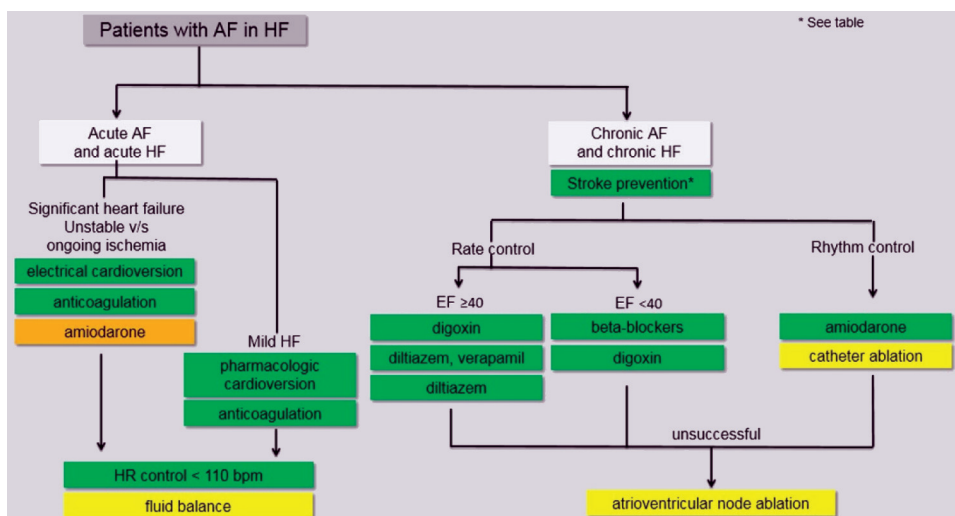


Figure 1. Rate control and rhythm control in patients with AF in HF.

AF=atrial fibrillation, EF=ejection fraction, HF=heart failure
 * Choose appropriate oral anticoagulant according to Table 3

those with and those without HF for freedom from AF after CA relative to HF status and significant LVEF improvement^(9,10). The largest meta-analysis on this topic revealed that the efficacy of CA in patients with AF improves significantly when performed early in the natural history of AF ($p=0.030$) and HF ($p=0.045$), and that CA yields long-term LVEF benefit, thus reducing the proportion of patients who would subsequently experience an LVEF decrease to less than 35% ($p<0.001$).

The Catheter Ablation for Atrial Fibrillation with Heart Failure (CASTLE-AF) trial randomly assigned patients with symptomatic paroxysmal or persistent atrial fibrillation that did not respond to antiarrhythmic drugs, had significant side effects, or were unwilling to take these drugs to undergo guideline-based therapy for heart failure and either catheter ablation or medical therapy (rate or rhythm control) for atrial fibrillation. The composite endpoint occurred in significantly fewer patients in the ablation group than in the medical therapy group (51 patients [28.5%] versus 82 patients [44.6%]; HR 0.62, 95% CI 0.43 to 0.87; $p=0.007$), and fewer patients in the ablation group died from any cause (24 patients [13.4%] versus 46 patients [25.0%]; HR 0.53, 95% CI 0.32 to 0.86; $p=0.01$)⁽¹¹⁾. Accordingly, catheter ablation should be considered a preferred treatment option in AF patients that are still symptomatic despite optimal medical therapy. Importantly, catheter ablation should be performed only at centers with trained, experienced, and well-

equipped teams.

In summary, in patients with AF in HF, rate control using beta-blocker and digitalis is appropriate in selected patients, with amiodarone as the next treatment option after considering the acceptability of the long-term side effects. Catheter ablation of AF or ablation of the AV node with subsequent pacemaker implantation may be indicated in patients with symptomatic or refractory AF.

Consensus statements

1. Most patients with HF (reduced or preserved EF) and AF will qualify for oral anticoagulation (either with VKAs or a NOAC) according to their CHA₂DS₂-VASc score and their level of bleeding risk (HAS-BLED score).
2. Rate control of AF is non-inferior to rhythm control, but rhythm control should be attempted in patients that are highly symptomatic.
3. Amiodarone is the drug of choice for rhythm control, whereas beta-blocker, digoxin, or their combination is recommended for rate control.
4. In patients with acute HF, rate control seems to be the preferred treatment strategy. However, after the acute phase of HF, the indication for rhythm control should be re-evaluated.
5. Beta-blockers do not alter prognosis in patients with concomitant HF and AF.
6. Catheter ablation may be considered for symptomatic patients with drug-refractory AF or in

selected patients.

7. In patients with therapy-refractory AF symptoms or uncontrolled heart rate, implantation of a biventricular pacemaker followed by AV node ablation (“pace and ablate”) should be considered.

8. Atrioventricular node ablation may also become necessary in HF patients on CRT therapy that develop permanent AF with ineffective biventricular pacing (fusion beats).

Conflicts of interest

The authors declare no conflict of interest.

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